

### **Integrated Science Assessments: The new NAAQS process**

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**Agency Problem/Client Need:** The Clean Air Act (CAA) mandates EPA to periodically review the scientific bases (“criteria”) for setting National Ambient Air Quality Standards (NAAQS) for the six major ambient air pollutants: particulate matter (PM), ozone (O<sub>3</sub>), lead (Pb), nitrogen oxides (NO<sub>x</sub>), sulfur oxides (SO<sub>x</sub>), and carbon monoxide (CO). The criteria must accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare that may be expected from the presence of such pollutant in the ambient air, in varying quantities. Historically, these findings were published in Air Quality Criteria Documents (AQCDs).

**Science Questions:** How to (1) complete NAAQS reviews on the 5-year cycle required by CAA, (2) include the most up-to-date scientific data, (3) characterize uncertainties in scientific/technical information, and (4) create a database to aid continuous identification of new studies?

**Approach:** An internal EPA workgroup developed a new NAAQS review process that, in consultation with the Clean Air Scientific Advisory Committee (CASAC) and interested stakeholders, includes the following key steps. Planning: Early in the process, the Office of Research and Development (ORD) and the Office of Air and Radiation (OAR) develop one integrated plan to guide the entire review. Science Assessment: An Integrated Science Assessment (ISA), a concise evaluation and synthesis of the most policy-relevant science with critical judgments relative to the criteria, is created. A state-of-the-art “evergreen” database will assist in preparing these assessments and allow broader access to information used in the ISA. Risk/Exposure Assessment: OAR will develop a concise document, informed by the ISA, focusing on key results, observations, and uncertainties. Policy Assessment/Rulemaking: An advance notice of proposed rulemaking (ANPR) containing a policy assessment that reflects Agency views will be published. The ANPR presents a range of policy options to inform the EPA Administrator’s decisions on retaining or revising the NAAQS. It describes the underlying interpretation of the scientific evidence and risk/exposure information that might support each option.

**Results/Outcomes:** ORD and OAR will have greater collaboration and coordination. Together they will hold initial workshops to receive input from experts, including CASAC members, to help formulate the draft integrated plan to guide the entire NAAQS review. The current O<sub>3</sub> NAAQS review will continue under the existing process, and a final rule is expected in March 2008. Transition to the new process began with the Pb NAAQS review, and an ANPR will be issued in November 2007 and a final rule in September 2008. Transition to the new process began earlier in the NO<sub>x</sub> and SO<sub>x</sub> reviews. Workshops were held in early 2007 to discuss key issues and initial draft chapters, which will be followed by an ISA, risk/exposure assessment report, policy assessment/ANPR (2009), notice of proposed rule (2009-2010), and notice of final rule (2010). The next PM NAAQS review will fully implement the new process. NCEA has conducted a needs assessment for the criteria pollutant database and is currently developing a prototype evergreen database, populating it with PM literature.

**Impacts:** This new process should allow completion of NAAQS reviews in a 5-year cycle, inclusion of the most up-to-date scientific information, and better characterization of uncertainties in information contained in the NAAQS review. It will also result in a close coupling of the ISA and the risk/exposure assessments.

## Atmospheric chemistry and physics used in Integrated Science Assessments

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**Agency Problem/Client Need:** The National Ambient Air Quality Standards (NAAQS) are set for six specific “criteria” pollutants that can act as indicators for mixtures of pollutants associated chemically or physically with the NAAQS. Thus, in addition to standards for the two single species carbon monoxide (CO) and lead (Pb), NAAQS are set for ozone (O<sub>3</sub>), the indicator for a mix of O<sub>3</sub> and other photochemical oxidants; for nitrogen dioxide (NO<sub>2</sub>), the indicator for a mix of nitrogen oxides; and for sulfur dioxide (SO<sub>2</sub>), the indicator for a mix of oxides of sulfur. Particulate matter (PM) standards involve additional complexity, because PM itself comprises many constituent chemical species distributed over several size ranges.

**Science Questions:** What physical and chemical transformations occur between source emissions and human or ecological receptors? How do atmospheric transformation reactions produce new chemical species from the emitted pollutants? Which intermediate and new end-product species are associated with each NAAQS indicator? Have the most useful species been identified as NAAQS indicators? How do atmospheric transformations affect the interpretation of epidemiological and toxicological studies, in particular, those relating health outcomes to pollutant sources?

**Approach:** NCEA’s atmospheric scientists formulate science questions related to setting NAAQS to support the NCEA health effects staff, the EPA program offices—chiefly OAQPS and other units of OAR—and several other EPA ORD centers and laboratories. We obtain ambient data from the most recent field studies, sometimes as participants, and from EPA’s regulatory ambient monitoring Air Quality System (AQS) database, using them together with statistical and numerical process models to characterize current ambient concentrations and to understand pollutant transformations and source-receptor relationships.

**Results/Outcomes:** Data compiled by NCEA atmospheric scientists suggest that systemic instrument error in the federal register method (FRM) results in a 20–25% positive artifact in NO<sub>2</sub> at typical urban levels due to higher-order nitrogen oxidation products. Work produced by Lamsal et al. in 2007 in collaboration with NCEA scientists used satellite column NO<sub>2</sub> to correct surface-based NO<sub>2</sub> data like those in AQS used for determining NAAQS compliance, making a significant improvement for estimating the actual levels of the NO<sub>2</sub> NAAQS indicator. In May 2002, NCEA atmospheric scientists collaborated with colleagues at NOAA and EPA NERL to collect data during field experiments in Tampa, FL. The month was then simulated by NCEA and NERL scientists using EPA’s Community Multi-scale Air Quality (CMAQ) modeling system, and model predictions were compared to observations. Judging CMAQ’s predictive skill in replicating the observed concentrations of these NAAQS pollutants is a crucial part of State Implementation Plans (SIPs) and of other planning and compliance tools used by OAQPS.

**Impacts:** The integration and analysis of atmospheric science data and modeling pertaining to physical and chemical processes occurring on NAAQS indicator species forms the opening section of NCEA’s ISAs and describes how pollutants are emitted, travel, and are transformed on the way from sources to human and ecological receptors. This work also characterizes how some pollutants act as surrogates or confounders in the mix of ambient atmospheric pollutants, as with the co-pollutants CO, PM, and NO<sub>2</sub> from auto traffic. Errors measuring low levels of some criteria pollutants can introduce additional uncertainty into some epidemiological studies. NCEA’s atmospheric science work to characterize this error is a significant part of EPA’s applied research to support health effects science. These results then influence EPA’s decisions on the choice of the form and atmospheric levels of the NAAQS indicator species, and on methods and instrumentation used in regulatory monitoring networks to establish compliance.

## Use of exposure science in the Integrated Science Assessments

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**Agency Problem:** Epidemiologic studies use ambient concentrations as indicators of personal exposure to the causal factors in evaluating associations of air pollutants with health effects. There has been concern that ambient concentrations might not adequately characterize personal exposures to particulate matter (PM) and other criteria pollutants. Therefore, a critical Agency need was to determine if ambient PM<sub>2.5</sub> concentrations could be used as a surrogate for exposure in order to support the use of epidemiologic study results to inform National Ambient Air Quality Standards (NAAQS) setting. Relationships among the various ambient concentration and exposure variables are also important in understanding the effects of exposure error on results of epidemiologic studies.

**Science Questions:** The overarching science question is should ambient concentration be considered a surrogate for total personal exposure, composed of ambient and nonambient components, or only for the ambient component of personal exposure? In other words, which is the most relevant exposure indicator for epidemiologic studies, total personal exposure or the ambient component? Related questions include what uncertainties are associated with the linkages among ambient concentrations and exposure variables? Do uncertainties in these linkages cause uncertainties in health effect estimates? Are variations in community average exposures adequately represented by variations in concentrations observed at ambient sites?

**Approach:** Information acquired through reviewing, analyzing, and interpreting pertinent scientific literature is used to prepare the Integrated Science Assessments (ISA). National Center for Environmental Assessment (NCEA) scientists conduct research on key issues in exposure assessment and publish key findings for use in future NAAQS reviews. NCEA scientists developed a technique to estimate personal exposures to ambient PM concentrations. Exposure panel studies relating ambient concentrations to personal exposures were reanalyzed to determine the validity of using ambient concentration as a surrogate for personal exposure in epidemiological studies. Cooperative studies were initiated to examine the spatial variability of ambient concentrations of PM<sub>2.5</sub>. A panel epidemiologic study was reanalyzed using ambient exposure instead of personal exposure. Measured personal ozone exposure concentrations were compared to those predicted from ambient concentrations using an exposure model.

**Results/Outcomes:** The technique developed to estimate the ambient and nonambient components of personal exposure to PM was used to show that ambient concentration is a good surrogate for exposure to the ambient component of personal exposure but not for either total personal exposure or its nonambient component. New information on the linkages among concentration and exposure variables were developed through NCEA-conducted research and analyses as part of NAAQS reviews. These new concepts have been presented at scientific meetings, published in the scientific literature, and used in NCEA assessments. NCEA scientists have taken a leadership role in educating the scientific public that ambient exposure, rather than total personal exposure, is associated with mortality and morbidity caused by ambient air pollution and is, therefore, the key variable for epidemiology.

**Impacts:** Exposure sections were prepared for previous NAAQS reviews. Work is beginning on exposure sections for the current PM ISA. NCEA scientists have played key roles in establishing that ambient exposures (rather than total personal exposures) are associated with health effects measured by community time-series epidemiology, and that these associations are not biased by nonambient exposures. The use of community time-series epidemiology for informing the NAAQS setting process is thus placed on a firm scientific basis.

## **Dosimetry of criteria pollutants in the Integrated Science Assessments**

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**Agency Problem/Client Need:** Dosimetry refers to the measurement or estimation of the amount of a pollutant and/or its reaction products reaching and persisting at specific sites in the respiratory tract. It is well established that health outcomes are associated with the dose of a compound to target tissues and not exposure per se. Dosimetric analyses establish the linkages between exposure and dose and toxicological effect. These analyses help bridge the gap between the laboratory setting and the ambient scenario under which people are exposed.

**Science Question(s):** To what degree does delivered dose affect the apparent susceptibility to a pollutant? How do physicochemical properties of pollutants affect the site and amount of the delivered dose? How much do rates of clearance, metabolism, and biochemical reactions influence health endpoints? Are reactions in the epithelial lining fluid protective? What are the dosimetric considerations for species-to-species extrapolations?

**Approach:** The major factors affecting the transport and fate of aerosols and gases in the respiratory tract are the lung morphology; route and rate of breathing; physical processes that govern gas transport and distribution in the lung; physiochemical properties of the mucous and surfactant layers; and physicochemical properties of the pollutant. Differences exist between and within species as a function of age, gender, and disease status must be carefully considered when seeking to integrate findings between studies and across disciplines.

**Results/Outcomes:** Particulate matter is used as an example of how dose, distribution of dose, and retention are affected by various factors. Some basic dosimetric issues are easily recognizable. For instance, rats are obligate nasal breathers, whereas humans breathe oronasally. Moreover, in humans, the total amount of air inhaled and the fraction entering via the mouth increase with activity and with respiratory disease severity. Such distinctions are important because the nasal passages remove a larger portion of inhaled pollutants than the oral passages. Thus, nasal breathing reduces the amount of a pollutant reaching the lower airways. Pulmonary defense mechanisms also vary among species, regions of the respiratory tract, and as a function of disease status and thus add to the complexity of dosimetric comparisons.

**Impacts:** Dosimetric analyses aid in the extrapolation of laboratory results to “real-world” conditions by considering how numerous factors contribute to the disposition of pollutants in the respiratory tract. Such analyses help to identify susceptible subgroups and associated risk factors and contribute to the overall interpretation and integration of data from human clinical studies, toxicological studies (in vivo, ex vivo, and in vitro), and epidemiologic studies. The use of dosimetry can improve both qualitative and quantitative risk analyses for inhaled pollutants.

## Use of epidemiology and human clinical studies in Integrated Science Assessments

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**Agency Problem/Client Need:** Observational epidemiological and controlled human exposure studies provide the most compelling evidence for air pollutant regulation, because direct effects on human health can be quantified. Careful integration and interpretation of results from a large number of human studies while considering the complexity of the information they provide is needed, however, to assess public health risks.

**Science Questions:** How can the body of literature on the human health effects of air pollution be used to (1) determine causality; (2) quantify exposure/concentration-response relationships; and (3) identify susceptible populations?

**Approach:** National Center for Environmental Assessment (NCEA) staff reviews the available literature to establish the scientific criteria for the National Ambient Air Quality Standards (NAAQS). Additional analyses are conducted as needed to aid in the interpretation of the available data. Examples of such additional analyses may include secondary analyses of published data or meta-analyses of exposure/concentration-response relationships. Understanding shifts in the population distribution of health outcomes associated with exposure to criteria air pollutants is critical for evaluating potential public health impacts of environmental exposures. NCEA analyses were conducted to evaluate such distribution shifts, because a seemingly small increase in a mean health outcome may push the most susceptible group in the population above a critical cut point on the continuum of disease development such that the disease may become clinically manifested. NCEA scientists also conduct analyses to summarize the available epidemiological literature, because studies may include results for multiple items of interest, be they pollutants, pollutant metrics, outcomes, cities, and/or lag structures. The large number of effect estimates reported in multiple studies can be summarized to allow for evaluation of consistency and coherence of findings across studies.

**Results/Outcomes:** Various epidemiologic and human clinical studies provide evidence for or against the need to revise or retain the NAAQS for a criteria air pollutant. NCEA scientists consider of the strengths and limitations, consistency, and robustness of the available evidence from those studies to characterize the pollutant concentrations at which human health effects are observed and to identify susceptible populations. In a December 2006 workshop, NCEA considered the cross-cutting methodological issues that can influence the interpretation of epidemiologic studies that use ambient air monitoring data.

**Impacts:** Assessments prepared by NCEA, with additional exposure and risk analyses conducted by the Office of Air Quality Planning and Standards (OAQPS), provide the major scientific and technical bases for EPA's decision to revise or retain the current NAAQS. For example, as a result of assessments prepared by NCEA, the 24-h PM<sub>2.5</sub> NAAQS was reduced in 2006 and a reduction in the ozone NAAQS was proposed in 2007. EPA's assessment of human studies, along with the judgment of Office of Research and Development (ORD) clinicians, epidemiologists, and other related experts, further serve as the bases for the Air Quality Indices and public communication materials available on the cross-agency AIRNow Website. These products are highly valued by state, local, and tribal agencies, other partners (e.g., National Oceanic and Atmospheric Administration (NOAA), media partners, and the public).

## **Particulate Matter Provisional Assessment: Health effects literature published 2002–2006**

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**Agency Problem/Client Need:** The EPA Administrator relies on NCEA's evaluation of the most current research findings in Air Quality Criteria Documents (AQCDs) when making decisions regarding National Ambient Air Quality Standards (NAAQS). The most up-to-date scientific literature was not included in the 2004 particulate matter (PM) AQCD, as there was a lag between the completion of the AQCD and the proposed rulemaking. During the rulemaking portion of the recent PM NAAQS review, EPA Administrator Steve Johnson asked NCEA to conduct a survey and provisional assessment of the numerous studies relevant to the health effects of PM that had been published since the 2004 PM AQCD was finalized.

**Science Questions:** What information does the new PM research provide regarding the components of NAAQS (i.e., indicator, averaging time, and level)? Do the results of these new studies differ greatly from the 2004 PM AQCD conclusions?

**Approach:** NCEA staff screened and reviewed the over 700 recently available PM health-related literature to identify potentially relevant studies. The studies likely to be most relevant were (a) epidemiologic studies that used PM<sub>2.5</sub> or PM<sub>10-2.5</sub> and were conducted in the United States or Canada and (b) toxicologic or epidemiologic studies that compared the effects of PM from different sources, with different components, collected in different locations, or contained different size fractions. About 200 key studies were identified and their findings summarized. NCEA staff then developed a Provisional Assessment that placed study results of potentially greatest significance in the context of the findings of the 2004 PM AQCD.

**Results/Outcomes:** The 2006 PM Provisional Assessment reported that newly identified studies expanded scientific information and provided important insights on the relationships between PM exposure and health effects. For example, the body of literature on coarse PM (between 2.5 and 10 µm in diameter) had grown substantially since the 2004 AQCD was released; however, the results from epidemiological and toxicological studies were mixed. In addition, many new studies had been published on specific particle sources and components that may contribute to adverse health effects. Nevertheless, taken in context, the new information and findings did not materially change any of the scientific conclusions regarding the health effects of PM exposure made in the 2004 PM AQCD.

**Impacts:** Information in the PM Provisional Assessment was used together with the PM AQCD and risk and exposure assessments completed by the OAQPS, to assist the EPA Administrator in making a final decision on the PM NAAQS. Based on these assessments, the Administrator promulgated a new 24-h standard for PM<sub>2.5</sub>, decreasing the level from 65 to 35 µg/m<sup>3</sup> and retained the annual standard of 15 µg/m<sup>3</sup>. The downward revision of the 24-h PM standard is estimated to result in substantial reductions in PM-related mortality and morbidity. The 2006 PM Provisional Assessment will provide the foundation for the Integrated Science Assessment (ISA) that will be a major element of the next review of the PM NAAQS that was begun in summer 2007.

## **Ozone Air Quality Criteria Document: Mechanisms underlying health effects**

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**Agency Problem/Client Need:** Congress mandates, through the Clean Air Act, that the EPA periodically review the scientific bases (or “criteria”) for setting National Ambient Air Quality Standards (NAAQS) for the six major pollutants, including ozone (O<sub>3</sub>). In 1971, the primary and secondary NAAQS for total photochemical oxidants were first promulgated at 0.08 ppm with a 1-h averaging time. In 1979, the standard was revised to 0.12 ppm. Following the 1997 review, a new daily maximum 8-h average standard of 0.08 ppm was promulgated for both the primary and secondary standards. A review of the O<sub>3</sub> NAAQS is currently underway.

**Science Questions:** Do adverse health effects occur at current O<sub>3</sub> ambient levels, including increases in mortality in exposed populations? What is the strength of evidence for associations between various endpoints and ambient O<sub>3</sub> concentrations? Do the results of O<sub>3</sub> toxicological and human clinical studies provide biologic plausibility and coherence for the variety of health effects observed in recent O<sub>3</sub> epidemiologic studies? How can mechanism-of-action information be used as part of the weight of evidence, to provide insight into potential relationships between or among observed health effects, and to understand how copollutant exposures may impact public health?

**Approach:** NCEA staff and approximately 20 academic and health researchers reviewed studies published since the last review in 1997. NCEA conducted additional data analyses to clarify key issues, weighed the scientific evidence, and published the findings in the O<sub>3</sub> Air Quality Criteria Document (AQCD). Two drafts of the AQCD were reviewed by the Clean Air Science Advisory Committee (CASAC), NHEERL scientists, and the public.

**Results/Outcomes:** Consistent, coherent effects were seen across a wide range of health outcomes. Several studies reported effects at levels below that of the current standard. New epidemiological studies add to previous evidence of O<sub>3</sub>-related respiratory morbidity effects, ranging from lung function decrements and symptoms to respiratory-related hospital admissions and emergency department visits. Large multicity studies, a number of single-city studies, and several meta-analyses provide evidence of a robust association between ambient O<sub>3</sub> and mortality. Persons with preexisting disease (especially asthma), children, and the elderly have been found to be more susceptible of O<sub>3</sub> health effects. New work has revealed that susceptibility is, in part, genetically determined.

**Impacts:** The O<sub>3</sub> AQCD along with the risk and exposure assessments prepared by OAQPS provide major scientific bases for EPA’s policy decision to revise or retain the current O<sub>3</sub> NAAQS. Based on these O<sub>3</sub> assessments, CASAC unanimously concluded that the standard “needs to be substantially reduced to protect human health, particularly in sensitive subpopulations.” Administrator Johnson also stated that based on the new analyses he believes the current standard is inadequate and proposed to set the primary (health) standard to a level within the range of 0.070–0.075 ppm. An analysis of the public health implications of a standard set at 0.070 ppm relative to current standard would result in: ~50–65% fewer children (all or asthmatic) estimated to experience moderate lung function decrements; ~20% fewer days of respiratory symptoms for asthmatic children; and 20–55% fewer O<sub>3</sub>-related deaths.

## Lead Air Quality Criteria Document: Effects below 10 µg/dL

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**Agency Problem/Client Need:** Lead (Pb) is one of the six major ambient air pollutants for which the Clean Air Act specifies that the EPA must periodically review the scientific bases (or “criteria”) for setting National Ambient Air Quality Standards (NAAQS). The 1977 Pb Air Quality Criteria Document (AQCD), based on research completed to that date, informed the Administrator’s decision to set the Pb standard at 1.5 µg/m<sup>3</sup>. That research showed subtle indicators of Pb intoxication at blood lead levels just above 30 µg/dL. A subsequent AQCD completed in 1986 (accompanied by a supplement published in 1990) reported health effects at levels of 10–15 µg/dL.

**Science Questions:** With the removal of Pb from most fuels and paint and the decrease in the number of smelters, Pb emissions have dropped, resulting in a decline in children’s concurrent blood Pb levels. Given this decline in Pb emissions and blood Pb, what are the health effects associated with current Pb exposures? At what blood Pb levels are these health effects observed? What are the sensitive subpopulations and how might they be differentially impacted?

**Approach:** NCEA staff and approximately 20 academic and health researchers reviewed over 6,000 newly available studies on the environmental and health effects of Pb. Drafts of the AQCD were reviewed by the Clean Air Science Advisory Committee (CASAC), National Health and Environmental Effects Research Laboratory (NHEERL) scientists, and the public.

**Results/Outcomes:** New evidence from NHEERL scientists and other researchers shows that blood Pb levels of <10 µg/dL (the current CDC action level) are associated with impaired neurocognitive ability (e.g., decreased IQ, attention deficits, antisocial behavior, low academic achievement) and also with altered immune function. In adults, blood Pb levels of <10 µg/dL are associated with enhanced risk of hypertension and renal dysfunction. Pb has negative effects on most organ systems including the cardiovascular, renal, immune, and reproductive systems.

**Impacts:** The Pb AQCD published in 2006, along with exposure and risk assessments prepared by OAQPS, NCEA’s client office, will provide major scientific bases for the EPA’s decision to revise or retain the current NAAQS for Pb. Information in the Pb AQCD is creating greater scientific and public awareness that the current CDC level of concern is not protective of public health. Effects identified the ISA will be a focal point of the decision-making. The Pb AQCD and associated assessments provide guidance for air quality managers, serve as a resource for states and international programs setting air quality standards and/or guidelines, and serve as a primary reference for the international research community.



## Oxides of Nitrogen Integrated Science Assessment: A focus on mixtures

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**Agency Problem/Client Need:** One of the principle considerations in the setting of the primary NAAQS for NO<sub>2</sub> is the issue of mixtures. Oxides of nitrogen are a complex mixture of NO<sub>x</sub> and NO<sub>z</sub>. Measurements of NO<sub>2</sub> in ambient air, used as an indicator for all oxides of nitrogen, are subject to interference by NO<sub>z</sub> compounds such as HNO<sub>3</sub> and PAN. Additionally, ambient NO<sub>2</sub> is highly correlated with other combustion-generated pollutants in urban areas and exhibits a pattern of spatial and temporal variability that is consistent with combustion-generated pollutant mixtures (including carbon monoxide [CO] and particulate matter [PM] species), making it difficult to distinguish health effects attributable to NO<sub>2</sub> from those attributable to other components in the mixture.

**Science Questions:** How well does the current monitoring system characterize concentrations of NO<sub>2</sub> for use in health-based studies? How can health-based effects associated with NO<sub>2</sub> be disentangled from those that could be attributed to other combustion-generated pollutant mixtures including CO and PM? Which health effects are independently associated with exposure to ambient concentrations of NO<sub>2</sub>?

**Approach:** The ISA synthesizes information on the health effects of NO<sub>x</sub>, drawing from several disciplines including atmospheric sciences, ambient monitoring, exposure assessment, dosimetry, animal toxicology, and human clinical studies and epidemiology. These lines of evidence are integrated to evaluate the consistency, coherence, and plausibility of health effects as observed at current ambient levels of NO<sub>2</sub>. The challenge is to interpret the available evidence on relationships between the measurements made at ambient monitoring sites and the health effects evaluated, and the public health significance of these outcomes.

**Results/Outcomes:** The 1993 AQCD for Oxides of Nitrogen identified two key health effects at ambient or near-ambient concentrations of NO<sub>2</sub>: (1) increases in airway responsiveness of asthmatic individuals after short-term exposures and (2) increased respiratory illness among children with longer-term exposures to NO<sub>2</sub>. Preliminary results from the first draft of the NO<sub>x</sub> ISA have confirmed and extended these conclusions. We are limited in our ability to evaluate NO<sub>2</sub> and other oxides of nitrogen as causal agents because of the correlations between NO<sub>2</sub> and other combustion-related pollutants. Despite the challenge of isolating NO<sub>2</sub> effects from effects associated with combustion-generated pollutant mixtures, especially traffic pollution, recent studies provide strong scientific evidence that NO<sub>2</sub> is associated with a range of respiratory effects. The available epidemiologic and toxicologic data provide suggestive evidence that long-term exposure to NO<sub>2</sub> affects respiratory health. Overall, the evidence is inconclusive with regard to the effect of NO<sub>2</sub> on the cardiovascular system and regarding the association between long-term exposure to NO<sub>2</sub> and mortality.

**Impacts:** The ISA, along with the risk/exposure and policy assessments prepared by the Office of Air and Radiation (OAR), Office of Air Quality Planning and Standards (OAQPS), will provide major scientific bases for EPA's decision to revise or retain the current NO<sub>2</sub> NAAQS. These assessments provide guidance for air quality managers, serve as a resource for states and international programs setting air quality standards and/or guidelines and serve as a primary reference for the international scientific community.

**Sulfur Oxides Integrated Science Assessment:  
Evaluating the concentration–time–response relationship in a susceptible population**

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**Agency Problem/Client Need:** The last review of the primary National Ambient Air Quality Standards (NAAQS) for sulfur dioxide (SO<sub>2</sub>) in 1996 resulted in the retention of the existing (1971) standards of 0.14 ppm (24-h limit) and 0.03 ppm (annual). In recent years, many of the annual and 1-h mean concentrations have been observed to be at or below operating levels of detection for the standard SO<sub>2</sub> monitor used in regulatory networks, limiting the ability of standard epidemiological methods and/or study designs to accurately characterize the concentration–time–response function.

**Science Questions:** How have recent decreases in ambient SO<sub>2</sub> concentrations impacted how we assess the health outcomes associated with SO<sub>2</sub> exposure? Is the current monitoring system sufficient to support the conclusions drawn from SO<sub>2</sub> epidemiologic studies? How does the new scientific evidence increase our understanding of the public health impacts of low ambient SO<sub>2</sub> concentrations? Can we adequately characterize the concentration–time–response relationship at low ambient SO<sub>2</sub> levels, including the identification of a population effect threshold, if it exists?

**Approach:** Health researchers from academia are working along with EPA staff on reviewing ~2,000 newly available studies (published from 1982-2007) on sulfur oxides (SO<sub>x</sub>) health effects. The Integrated Science Assessment (ISA) for SO<sub>x</sub> will present the most pertinent new health evidence in support of the primary NAAQS review. The ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) and the public, with the final version due out in 2008.

**Results/Outcomes:** Techniques currently used for regulatory ambient monitoring of SO<sub>2</sub> are inadequate for precise measurements: the lower limits of detection (LOD) are at or near the current mean 24-h ambient SO<sub>2</sub> levels (~3 ppb). The EPA is engaged in a program to install newer trace-level SO<sub>2</sub> instruments that will increase the precision of observations at low ambient levels; however, this initiative will not provide information for the current NAAQS review. Evaluation of the epidemiological evidence indicates that individuals with respiratory illnesses, particularly asthma, are more susceptible to respiratory health effects from SO<sub>2</sub> exposures than the general public. In human clinical studies, significant decreases in pulmonary function and increases in respiratory symptoms have consistently been demonstrated in exercising asthmatics following 5- to 15-min peak exposures to 0.5- to 1.0-ppm SO<sub>2</sub>. In some asthmatics, these effects have been observed following peak exposures to concentrations of as low as 0.25 ppm. The observations in human clinical studies of increased sensitivity to SO<sub>2</sub> exposures in asthmatic subjects compared to healthy subjects provide coherence and biological plausibility for the respiratory effects observed in epidemiological studies. However, identifying possible thresholds in epidemiological studies is challenging due to low data density in the lower concentration range, measurement error in response or exposure, and shallow slope near any threshold that might exist.

**Impacts:** Although SO<sub>2</sub>-related health risk estimates may appear to be small, they may well be significant from an overall public health perspective because of the large numbers of individuals exposed and the size of the at-risk population.

## **Oxides of Nitrogen and Sulfur Oxides Integrated Science Assessment of the secondary standard: Ecological effects**

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**Agency Problem/Client Need:** In the Integrated Science Assessment (ISA) for nitrogen oxides (NO<sub>x</sub>) and sulfur oxides (SO<sub>x</sub>), NCEA is evaluating the environmental effects of NO<sub>x</sub> and SO<sub>x</sub> in tandem as part of a joint review of the secondary National Ambient Air Quality Standards (NAAQS) for NO<sub>2</sub> and SO<sub>2</sub>. EPA has recognized the merits of conducting an integrated review of these secondary standards to take into consideration the complex interrelationships between these pollutants. This multipollutant approach is designed to address acidification of ecosystems, a process that is driven by exposure to both NO<sub>x</sub> and SO<sub>x</sub>. Acidification causes a cascade of effects that harm terrestrial and aquatic ecosystems and include slower growth, injury or death of forests, and localized extinction of fish and other aquatic species. In addition to acidification, NO<sub>x</sub> act in concert with other sources of reactive nitrogen (fertilizers, sewage, and atmospheric NH<sub>x</sub>) to cause "nitrogen pollution," resulting in a suite of terrestrial and aquatic ecological problems, including biodiversity losses, disease, eutrophication, and harmful algal blooms. Lastly, SO<sub>x</sub> interact with mercury (Hg) in ecosystems to increase the production of methylmercury, a powerful toxin that bioaccumulates, often causing toxic doses to top members of food webs (e.g., river otters, kingfishers, panthers).

**Science Questions:** Are there robust concentration-response relationships or simple associations between deposition and ecological responses? At what scale do we want to focus protection (e.g., whole ecosystems, individual species, biological diversity)? How can the scientific evidence inform evaluation of potential indicator(s) for environmental impacts?

**Approach:** NCEA staff and approximately 30 researchers from academic, private, and federal research organizations are currently reviewing thousands of peer-reviewed publications on the environmental effects of NO<sub>x</sub> and SO<sub>x</sub>. These references have become available since the last NO<sub>x</sub> and SO<sub>x</sub> Air Quality Criteria Documents (AQCDs) were published in 1992 and 1982, respectively. Comprehensive reviews will be presented in the ISA annexes, while the ISA itself serves to report the most policy-relevant information.

**Results/Outcomes:** The initial draft of the NO<sub>x</sub>/SO<sub>x</sub> ISA is in development and will be released for the Clean Air Science Advisory Committee (CASAC) and public comment in December 2007. Preliminary findings indicate that acidification continues to degrade sensitive ecosystems throughout the United States. However, emission control strategies have reduced sulfate deposition in the eastern half of the country and have contributed to some aquatic systems showing signs of recovery. Nitrogen deposition contributes to eutrophication in estuarine and coastal ecosystems, especially on the East and Gulf Coasts.

**Impacts:** The NO<sub>x</sub>/SO<sub>x</sub> ISA provides the scientific underpinnings for the risk/exposure and policy assessments prepared by the Office of Air and Radiation (OAR), Office of Air Quality and Planning Standards (OAQPS) and will serve as the knowledge base for EPA's decision to revise or retain the current NAAQS. The ISA provides guidance for air quality managers, serves as a resource for states and international programs involved in setting air quality standards or guidelines, and is the authoritative reference for the international scientific community.

### Data resources supporting Integrated Science Assessments

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**Agency Problem/Client Need:** NCEA serves as a key component to the National Ambient Air Quality Standards (NAAQS) process for six criteria air pollutants: particulate matter, ozone, lead, nitrogen oxides, sulfur oxides, and carbon monoxide. EPA recently changed the process of reviewing the NAAQS to help meet the mandated 5-year schedule. Included in this set of revisions is the development of Integrated Science Assessments (ISAs), which are concise syntheses of the most policy-relevant science that critically evaluate scientific information on the human health and welfare effects related to these criteria pollutants. There is a need for the ISA to be linked to an electronic database of scientific studies. The development, implementation, and maintenance of such a database will facilitate a more continuous process to identify, compile, characterize, and prioritize new scientific studies.

**Science Questions:** How can an evergreen database support the ISA process and aid in streamlining the process of reviewing and revising the NAAQS? What resources already exist that can be used as a base for an evergreen database? How can an evergreen database serve as a resource to the overall scientific community?

**Approach:** Timely development of the ISA will be facilitated by a database that stores, organizes, and allows analysis of the scientific basis for each NAAQS. This evergreen database would encompass the entire breadth of information used in assessing the state of the science on exposure, ecological effects, and health effects (epidemiological, clinical, and toxicological). Towards this end, we have completed a Needs Assessment to evaluate currently existing databases within NCEA that proposes a database design that outlines maintenance and optimization support, creating public access to the database and quality assurance/quality control (QA/QC) procedures. Current projects include the evaluation of the Exposure-Response Database (ERDB), which houses animal toxicological and human clinical data and the creation of the Health Exposure Research Online (HERO) Database for epidemiological data. Future endeavors include designing a blueprint of a database that will house ERDB and HERO and accommodate the future needs for Ecologic and Exposure Assessment databases and eventually developing and implementing a large database that can be used by NCEA, throughout EPA, and by the public.

**Results/Outcomes:** The Needs Assessment has been completed and results are being incorporated into the design of a larger database. ERDB has been revised and the structure has been updated. It has been available as a Web-based interface since early 2007. We have completed beta testing of the HERO database. Data have been extracted from 235 epidemiological studies onto paper forms, which currently are being entered into HERO.

**Impacts:** The creation of an evergreen database will make the NAAQS process more efficient by providing the tools that NCEA scientists need to conduct, identify, catalog, and analyze the science that serves as a base for the ISA. The ERDB and HERO are key components to the development of the evergreen database, which will serve as a resource for states and international programs, such as the World Health Organization, in setting air quality standards or guidelines and a primary reference for the scientific community.